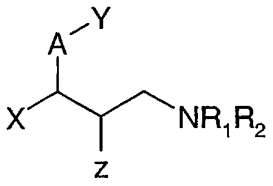
Claims

1. A compound of formula I:



I

wherein

A is selected from O and S;

X is selected from

phenyl optionally substituted with up to 5 substituents each independently selected from halo, C_1-C_4 alkyl and C_1-C_4 alkoxy;

thienyl optionally substituted with up to 3 substituents each independently selected from halo and C_1-C_4 alkyl; and

C_2-C_8 alkyl, C_2-C_8 alkenyl, C_3-C_8 cycloalkyl and C_4-C_8 cycloalkylalkyl, each of which may be optionally substituted with up to 3 substituents each independently selected from halo, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 alkyl-S(O)n- where n is 0, 1 or 2, $-CF_3$, -CN and $-CONH_2$;

Y is selected from phenyl, naphthyl, dihydrobenzothienyl, benzothiazolyl, benzoisothiazolyl, quinolyl, isoquinolyl, naphthyridyl, thienopyridyl, indanyl, 1,3-benzodioxolyl, benzothienyl, indolyl and benzofuranyl, each of which may be optionally substituted with up to 4 or, where possible, up to 5 substituents each independently selected from halo, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 alkyl-$S(O)_n$- where n is 0, 1 or 2, nitro, acetyl, $-CF_3$, $-SCF_3$ and cyano; and when Y is indolyl it may be substituted or further substituted by an N-substituent selected from C_1-C_4 alkyl;

Z is selected from OR_3 or F, wherein R_3 is selected from H, C_1-C_6 alkyl and phenyl C_1-C_6 alkyl;

R_1 and R_2 are each independently H or C_1-C_4 alkyl;

or a pharmaceutically acceptable salt thereof

with the proviso that when Y is optionally substituted phenyl or optionally substituted 1,3-benzodioxolyl and Z is OR_3 and X is optionally substituted phenyl then A is S.

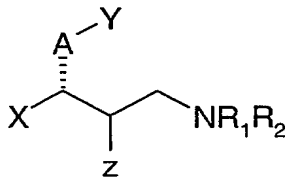
2. A compound as claimed in claim 1, wherein A is O.

3. A compound as claimed in claim 1, wherein A is S.

4. A compound as claimed in any one of the preceding claims, wherein one of R_1 and R_2 is H.

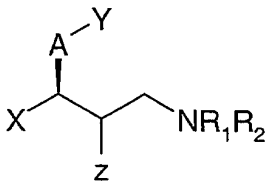
5. A compounds as claimed in any one of the preceding claims, wherein one of R_1 and R_2 is H and the other is methyl.

6. A compound as claimed in any one of the preceding claims, wherein the compound possesses the stereochemistry defined in formula II



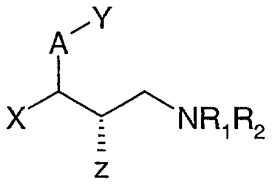
II

7. A compound as claimed in any one of claims 1 to 5, wherein the compound possesses the stereochemistry defined in formula III



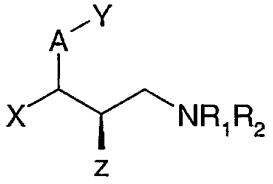
III

8. A compound as claimed in any one of claims 1 to 5, wherein the compound possesses the stereochemistry defined in formula IV



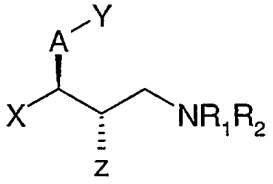
IV

9. A compound as claimed in any one of claims 1 to 5, wherein the compound possesses the stereochemistry defined in formula V



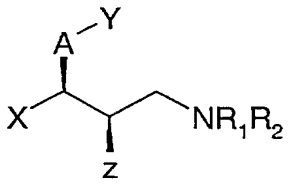
V

10. A compound as claimed in claim 7 or claim 8, wherein the compound possesses the stereochemistry defined in formula VI



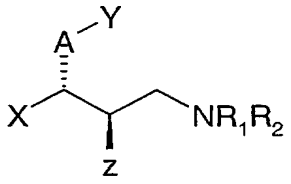
VI

11. A compound as claimed in claim 7 or claim 9, wherein the compound possesses the stereochemistry defined in formula VII



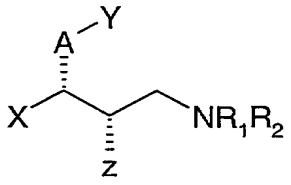
VII

12. A compound as claimed in claim 6 or claim 9, wherein the compound possesses the stereochemistry defined in formula VIII



VIII

13. A compound as claimed in claim 6 or claim 8, wherein the compound possesses the stereochemistry defined in formula IX



IX

14. A compound as claimed in any one of the preceding claims wherein Z is F.

15. A compound as claimed in any one of claims 1 to 13 wherein Z is OH.

16. A compound as claimed in any one of claims 1 to 13 wherein Z is OMe or OCH_2Ph.

17. A compound as claimed in any one of the preceding claims, wherein X is unsubstituted phenyl or phenyl which is mono-, di- or tri-substituted with substituents independently selected from halo, C_1-C_4 alkyl and C_1-C_4 alkoxy.

18. A compound as claimed in claim 17, wherein X is unsubstituted phenyl or phenyl which is mono-substituted with fluorine.

19. A compound as claimed in any one of the preceding claims, wherein Y is phenyl optionally substituted with up to 5 substituents each independently selected from halo, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 alkyl-$S(O)_n$- where n is 0, 1 or 2, nitro, acetyl, -CF_3, -SCF_3 and cyano.

20. A compound as claimed in claim 19, wherein Y is unsubstituted phenyl or phenyl which is mono-substituted with chlorine.

21. A compound as claimed in any one of the preceding claims, wherein Y is naphthyl optionally substituted with up to 5 substituents each independently selected from halo, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 alkyl-$S(O)_n$- where n is 0, 1 or 2, nitro, acetyl, -CF_3, -SCF_3 and cyano.

22. A compound as claimed in claim 21, wherein Y is unsubstituted naphthyl or naphthyl which is mono-substituted with fluorine.

23. A compound as claimed in claim 21 or 22, wherein the point of attachment of the optionally substituted naphthyl group to the O or S atom is attachment at the 1 position.

24. A compound as claimed in any one of the claims 1-18, wherein Y is benzofuranyl optionally substituted with up to 5 substituents each independently selected from halo, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 alkyl-$S(O)_n$- where n is 0, 1 or 2, nitro, acetyl, -CF_3, -SCF_3 and cyano.

25. A compound as claimed in claim 24, wherein Y is unsubstituted benzofuranyl or benzofuranyl which is mono-substituted with CH_3.

26. A compound as claimed in any one of the claims 1-18, wherein Y is benzothienyl optionally substituted with up to 5 substituents each independently selected from halo,

C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 alkyl-$S(O)_n$- where n is 0, 1 or 2, nitro, acetyl, -CF_3, -SCF_3 and cyano.

27. A compound as claimed in claim 26, wherein Y is unsubstituted benzothienyl or benzothienyl which is mono-substituted with fluorine.

28. A compound as claimed in any one of the claims 1-18, wherein Y is benzoisothiazolyl optionally substituted with up to 4 substituents each independently selected from halo, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 alkyl-$S(O)_n$- where n is 0, 1 or 2, nitro, acetyl, -CF_3, -SCF_3 and cyano.

29. A compound as claimed in any one of claims 24-28, wherein the point of attachment of the group Y to the O or S atom is attachment at the 7 position.

30. A compound as claimed in any one of claims 24-28, wherein the point of attachment of the group Y to the O or S atom is attachment at the 4 position.

31. A pharmaceutical composition comprising a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-30, together with a pharmaceutically acceptable diluent or carrier.

32. A compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-30, for use as a pharmaceutical.

33. A compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-30, for use as a selective inhibitor of the reuptake of both serotonin and norepinephrine.

34. A compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-30, for use in the treatment of a disorder associated with serotonin and norepinephrine dysfunction in mammals.

35. A compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-30, for use in the treatment of a disorder selected from depression, OCD, anxiety, memory loss, urinary incontinence, conduct disorders, ADHD, obesity, alcoholism, smoking cessation, hot flushes/flashes and pain.

36. The use of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-30, for the manufacture of a medicament for selectively inhibiting the reuptake of serotonin and norepinephrine.

37. The use of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-30, for the manufacture of a medicament for the treatment of a disorder associated with serotonin and norepinephrine dysfunction in mammals.

38. The use of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-30, for the manufacture of a medicament for the treatment of a disorder selected from depression, OCD, anxiety, memory loss, urinary incontinence, conduct disorders, ADHD, obesity, alcoholism, smoking cessation, hot flushes/flashes and pain.

39. The use as claimed in claim 38, wherein the disorder is selected from depression, urinary incontinence and pain.

40. A method for selectively inhibiting the reuptake of serotonin and norepinephrine in mammals, comprising administering to a patient in need thereof an effective amount of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-30.

41. A method for treating disorders associated with serotonin and norepinephrine dysfunction in mammals, comprising administering to a patient in need thereof an effective amount of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-30.

42. A method for treating a disorder selected from depression, OCD, anxiety, memory loss, urinary incontinence, conduct disorders, ADHD, obesity, alcoholism, smoking cessation, hot flushes/flashes and pain comprising administering to a patient in need thereof an effective amount of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-30.

43. The use as claimed in any one of claims 36-39, wherein the disorder is pain.

44. A method as claimed in any one of claims 40-42, wherein the disorder is pain.